

DSFEHEVWQD ASSFRLIFIV DVWHPELTPO QRRSLPAI (SEQ ID NO:2; GENBANK
Accession No. S83325; His motif is underlined; conserved
sequences within the catalytic domain are designated by bold
type)

5 For example, a compound which inhibits HAAH
hydroxylation is a polypeptide that binds a HAAH ligand but
does not transduce an intracellular signal or an polypeptide
which contains a mutation in the catalytic site of HAAH.
Such a polypeptide contains an amino acid sequence that is
10 at least 50% identical to a naturally-occurring HAAH amino
acid sequence or a fragment thereof and which has the
ability to inhibit HAAH hydroxylation of substrates
containing an EGF-like repeat sequence. More preferably,
the polypeptide contains an amino acid sequence that is at
15 least 75%, more preferably at least 85%, more preferably at
least 95% identical to SEQ ID NO:2.

20 A substantially pure HAAH polypeptide or HAAH-
derived polypeptide such as a mutated HAAH polypeptide is
preferably obtained by expression of a recombinant nucleic
acid encoding the polypeptide or by chemically synthesizing
the protein. A polypeptide or protein is substantially pure
when it is separated from those contaminants which accompany
it in its natural state (proteins and other naturally-
occurring organic molecules). Typically, the polypeptide is
25 substantially pure when it constitutes at least 60%, by
weight, of the protein in the preparation. Preferably, the
protein in the preparation is at least 75%, more preferably
at least 90%, and most preferably at least 99%, by weight,
HAAH. Purity is measured by any appropriate method, e.g.,
30 column chromatography, polyacrylamide gel electrophoresis,
or HPLC analysis. Accordingly, substantially pure
polypeptides include recombinant polypeptides derived from a
eucaryote but produced in *E. coli* or another procaryote, or

6-26-06
my

09903023-071101